

**Notice of Allowability**

Application No.

10/611,748

Examiner

Ashwin Mehta

Applicant(s)

YADAV, NARENDRA S.

Art Unit

1638

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to papers filed 20 March 2007 and tel. int. 21 May 2007.
2. ☒ The allowed claim(s) is/are 1,5,6,8,13-16 and 18-26.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |  |  |
|--|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)   | 5. <input type="checkbox"/> Notice of Informal Patent Application  |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date <u>attached</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br>Paper No./Mail Date _____    | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment  |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance                         |
|  | 9. <input type="checkbox"/> Other _____.   |

***Allowable Subject Matter***

1. The amendment filed 20 March 2007 has been entered. Amended claims 14-20 are joined with elected Group I and examined in this Office action.
2. The objection to claim 23 is withdrawn, in light of the claim amendment.
3. The rejections of claims 1-3, 5, 6, 8, 13, and 21-26 under 35 U.S.C. 112, second paragraph are withdrawn due to the claim amendment or upon further consideration.
4. The rejections of claims 1-3, 5, 6, 8, 13, and 21-26 under 35 U.S.C. 103(a) are withdrawn, upon further consideration of Applicant's argument that motivation is lacking for modifying the system taught by Smith et al. with a site-specific recombination system.

***Examiner's Amendment***

5. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Virginia Dress on May 21, 2007.

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The claims have been amended as follows:

1. A gene silencing site-specific recombination system

comprising:

a) a first recombinase element having the general structure P1-R,

wherein P1 is a first promoter and R is a recombinase coding sequence and 3' region; and

b) a second recombinase element having the general structure: RS-X-RS\*-Y

wherein:

i) RS and RS\* are opposingly oriented recombinase sites

responsive to the recombinase;

ii) X is a nucleic acid fragment comprising at least one second

promoter in a 3' to 5' orientation, wherein X comprises 5' Intron-TSINV-

P2INV; and

iii) Y is a nucleic acid fragment comprising [at least one target

sequence directed to a target gene, wherein Y comprises] 3' Intron-

TSINV-polyA;

wherein:

1) P2INV comprises an inverted second promoter whose

orientation is from 3'-5';

2) TSINV is an inverted target sequence whose orientation is from 3'-5', and is

complementary to a sequence in the coding region of a target gene;

3) polyA is the 3' region of a gene;

4) 5' Intron is the N-terminal portion of an intron; and,

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5) 3' Intron is the C-terminal portion of said [an] intron;  
wherein, when said system is present in a plant cell comprising the target gene, expression of the recombinase results in inversion of X, yielding a recombined second recombinase element, RS-P2-TS-5'Intron-RS\*-3' Intron-TSINV-polyA, wherein transcription of TS and TSINV by P2 results [the element contained between RS and RS\* and transcription of the inverted second recombinase element resulting] in the production of double-stranded RNA that causes [and] silencing of the target gene.

Claims 2 and 3 were cancelled.

In claim 5, line 4, --and-- was inserted before "Gin/gix" and ", a pSR1 system, a cer system, and a fim system" was deleted.

Claims 7, 9, and 10 were cancelled.

8. A gene silencing site-specific recombination system comprising:

a) a first recombinase element having the general structure P1-R, wherein P1 is a first promoter and R is a recombinase coding sequence and 3' region; and

b) a second recombinase element having the general structure

RS-5' Intron-TSINV- P2INV-RS\*-3' Intron-TSINV-polyA, wherein:

i) RS and RS\* are opposingly oriented recombinase sites responsive to the recombinase;

ii) 5' Intron is the N-terminal portion of an intron;

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iii) TSINV is an inverted target sequence and whose orientation is from 3'-5', and is complementary to a sequence in the coding region of a target gene [wherein the target sequence is directed to a target gene];

iv) P2INV is an inverted second promoter whose orientation is from 3'-5';

v) 3' Intron is the C-terminal portion of said [an] intron; and

vi) polyA is the 3' region of a gene;

wherein, when the system is present in a plant cell comprising the target gene, recombinase expression results in recombination of the second recombinase element to yield RS-P2-TS-5'Intron-RS\*-3' Intron-TSINV-polyA, wherein P1 and P2 are operably linked to their downstream elements, wherein following [and wherein expression of the recombinase results in inversion of the element contained between RS and RS\* and] transcription of the recombined [inverted] second recombinase element, [resulting in excision of] the intron is excised by mRNA splicing and the transcripts of TS and TSINV hybridize to form a [production of] double-stranded RNA that causes [and] silencing of the target gene.

In claim 13, line 2, the recitation, "any one of claims 8-10" was replaced with --claim 8--.

14. The gene silencing site-specific recombination system according to Claim 13 wherein the germline promoter is selected from the group consisting of:

[a) constitutive plant promoters;

b) plant tissue-specific promoters;

c) plant developmental stage-specific promoters;

- d) chemically-inducible plant promoters;
- e) viral promoters;]
- [f)] male germline-specific promoters;
- [g)] female germline-specific promoters;
- [h)] common germline-specific promoters;
- [i)] floral common germline-specific promoters;
- [j)] vegetative shoot apical meristem-specific promoters; and
- [k)] floral shoot apical meristem-specific promoters.

Claim 17 was cancelled.

In claim 18, line 2, "17" was replaced with --14--.

In claim 21, line 2, the recitation, "any of Claims 7-9" was replaced with --claim 8--; in lines 2-3, the recitation, "and optionally, third promoter, are" was replaced with --is--.

In claim 22, line 2, the recitation, "any of Claims 1, 4, and 7-9" was replaced with --claim 1 or claim 8--.

In claim 24, line 2, the recitation, "any of Claims 7-9" was replaced with --claim 8--; in line 4, --and-- was inserted before "Gin/gix"; in lines 4 and 5, the recitation, "a pSR1 system, a cer system, and a fim system" was deleted.

In claim 25, line 2, the recitation, “any of Claims 7-9” was replaced with --claim 8--.

In claim 26, lines 3-4, the recitation, “and reside in different plants” was deleted.

6. Claims 1, 5, 6, 8, 13-16, and 18-26 are allowed.

7. The following is an examiner’s statement of reasons for allowance: Applicants have developed a gene silencing site-specific recombination system, wherein the expression of nucleotide sequences that cause post-transcriptional silencing of a desired target gene is controlled with the use of a site-specific recombinase. The RNA encoded by the system that causes the silencing forms a hairpin loop, wherein one of the arms of the hairpin is complementary to RNA encoded by the target gene, and wherein the loop region of the hairpin is a spliceable intron. The system comprises a first recombinase element, that comprises a first promoter operably linked to the coding sequence of a site-specific recombinase, and a second recombinase element, having the structure, RS-5’ Intron-TSINV-P2INV-RS\*-3’ Intron-TSINV-polyA. RS and RS\* are opposingly oriented recombinase sites. The site-specific recombinase encoded by the first recombinase element will invert the nucleotide sequences flanked by RS and RS\*. TSINV encodes the target sequence that causes the silencing of the target gene when

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expressed as a double-stranded RNA. P2INV is a second promoter, in 3'-5' orientation. When present in a plant cell, expression of the recombinase will invert the sequence between RS and RS\*, and the recombined second recombinase element will then have the structure RS-P2-TS-5' Intron-RS\*-3' Intron-TSINV-polyA, and will express said hairpin loop that causes silencing of the target gene.

The Office action mailed September 27, 2006 included an obviousness rejection of the claims over Smith et al. (Nature, 2000, Vol. 407, pages 319-320) in combination with Odell et al. (WO 91/09957). In the response filed March 20, 2007, Applicants argued that just because one could modify Smith et al., one would not be lead to select Odell et al. for the modification (response, paragraph bridging pages 15-16). Applicant's argument was found persuasive. The prior art fails to suggest splitting an intron, placing one part of it in inverse orientation, and inverting it to make a complete intron using a site-specific recombination system, in a construct intended to express an RNA that forms a hairpin loop.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

#### ***Contact Information***

Any inquiry concerning this or earlier communications from the Examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The Examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Anne Marie Grunberg, can be reached at 571-272-0975. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can



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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

May 22, 2007



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